Fatal, incidental, idiopathic pulmonary fibrosis in a patient receiving long-term low-dose methotrexate for psoriasis

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Fatal, incidental, idiopathic pulmonary fibrosis in a patient receiving long-term low-dose methotrexate for psoriasis

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Methotrexate has historically thought to be able to cause pulmonary fibrosis and this potential side effect is listed in major textbooks, patient information leaflets and national guidelines.[1] This belief is based on a very small number of previously published isolated case reports; however, when these reports are scrutinised, such cases of pulmonary fibrosis arising many years after the introduction of methotrexate

could represent other interstitial lung diseases unrelated to methotrexate.[2,3] Once dogma is established, it can be difficult to undo.

An 83-year-old man was admitted with dyspnoea and a productive cough. Chest x-ray and high resolution CT demonstrated extensive pulmonary fibrosis with superimposed pneumonia. Medical history included previous cigarette smoking and methotrexate therapy for 10 years for psoriasis (average weekly dose of 5mg) which was stopped. He improved with initial treatment but had residual persistent significant respiratory failure and pulmonary hypertension requiring long-term home oxygen. He died 10 months later. The cause of death was considered to be idiopathic pulmonary fibrosis – the commonest form of interstitial lung disease but his family were concerned that the methotrexate he had been taking was to blame..

Interstitial lung disease (ILD) encompasses a large and heterogeneous group of parenchymal lung disorders, which overlap in their clinical presentations and patterns of lung injury.[4] Types of progressive ILD include autoimmune eg. associated with rheumatoid arthritis, Sjogren's syndrome, systemic sclerosis or dermatomyositis; pulmonary sarcoidosis, and exposure-related eg. inhalation of asbestos or silica.[4] Pathogenetic mechanisms are complex and research is ongoing to attempt to clarify areas of uncertainty including identifying markers / predictors of disease progression, selection of patients for treatment and the role of immunosuppressive therapy and antifibrotic therapy.[4]

In recent years, higher quality evidence has demonstrated a lack of association between methotrexate and pulmonary fibrosis.[5,6] However, acute pulmonary toxicity in the form of interstitial pneumonitis is a recognised very rare side-effect which is idiosyncratic and almost always presents within the first 12 months of methotrexate therapy with dyspnoea, cough and fever with systemic upset. On cessation of

methotrexate and appropriate acute treatment, the clinical features usually resolve and there are no long term sequelae. However, there are isolated reports of methotrexate-associated pneumonitis not responding to drug cessation and active treatment and so it is important that patients stop methotrexate and seek a medical assessment if they develop respiratory symptoms.

We wish to raise awareness of the possibility of coexisting pulmonary fibrosis with psoriasis and methotrexate therapy and to emphasise the lack of causation. We recommend that guidelines and information leaflets are updated to reflect expert respiratory medicine opinion and the latest evidence to avoid confusion and distress to patients and their families and prescribers of methotrexate. Interestingly, package leaflets for methotrexate and the main UK rheumatology charity organisation “Versus Arthritis” do not mention pulmonary fibrosis as a side effect but rather “fluid on the lungs” and “inflammation of the lungs” which is an accurate description of pneumonitis. It is very important to differentiate pneumonitis from fibrosis as prognosis is different. One must also not falsely implicate blame on a medication.

We advocate removing pulmonary fibrosis as a listed side-effect of low-dose weekly methotrexate therapy. Acute lung toxicity in the form of pneumonitis should continue to be stated as a rare side-effect.

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